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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,200	01/03/2003	Peter D. Kwong	54203-H-PCT-US/JPW/SHS	3857

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EXAMINER	
KIM, ALEXANDER D	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/856,200	KWONG ET AL.	
	Examiner	Art Unit	
	Alexander D. Kim	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,38 and 97-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-38 and 97-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office actions, a Non-Final rejection (mailed on 05/15/2006), Applicants filed a response and amendment received on 11/20/2006. Said amendment cancelled Claims 1-36 and 39-96, and added new Claims 97-106. Thus, Claims 37-38 and 97-106 are pending in the instant Office action.

Withdrawn-Compliance with Sequence Rules

2. The Sequence Non-compliance because of missing Sequence Listing is withdrawn by filing of Sequence Listing on 11/20/2006.

3. The Sequence Non-compliance in Figures 29D-1 and 29D-2 is withdrawn by the virtue of applicants' amendment.

4. The Sequence Non-compliance in structural coordinates of Figures 53-14 to 53-111 is withdrawn by the virtue of applicants' amendment.

Withdrawn-Objections to the Specification

5. Previous objection of the Title is withdrawn by virtue of Applicant's amendment.

6. Previous objection of the Abstract is withdrawn by virtue of Applicant's amendment.

Withdrawn-Claim Rejections - 35 USC § 112

7. Previous rejection of Claims 37 and 38 under 35 U.S.C. § 112, second paragraph, because of the use of the term "portion" or "portion of gp120" is withdrawn by the virtue of Applicants' amendment.

8. Previous rejection of Claims 37 and 38 under 35 U.S.C. § 112, second paragraph, because it is unclear as to how a skilled artisan is to determine a binding site, determine whether a compound would fit, and/or design a compound as encompassed by the claims is withdrawn by the virtue of Applicants' amendment.

New-Claim Rejections - 35 USC § 112

10. Claims 37-38 and 97-106 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. This rejection is necessitated by the amendment. The phrases "a resolution better than 2.5 Angstroms" in claims 37, 38, 97-100 (claims 101-106 dependent therefrom) are unclear as to the limitations they impart on the claimed subject matter or as to what said phrases encompass and one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed crystals. It is well known in the art that the smaller the number (i.e. Angstroms), the higher the resolution. In this case, the term can be interpreted in the following two distinct ways: 1) a resolution of a number equal to or greater than 2.5 Å, which is a

lower resolution or 2) a resolution of a number equal to or less than 2.5 Å, which is a higher resolution. Clarification is required.

9. Claims 37-38, 97-98 and 101-104 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by the amendment. Claims 37-38 and 97-98 (claims 101-104 dependent therefrom) recite the limitation of amino acid residues, "83-127", "195-302", "330-492" in Claim 37, for example, which is a relative term. The amino acid residue number used in the claims to describe specific amino acid residues is unclear without the point of reference, preferably identified by SEQ ID NO. Clarification is required.

10. Claims 37, 97, 99, 101, 103 and 105 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by the amendment. Claims 37, 97 and 99(claims 101, 103 and 105 dependent therefrom) recite the limitation "positive fitting". The term "positive fitting" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is wholly unclear how a compound would be considered to have "positive fitting" into the binding site. Clarification is required.

Maintained - 35 U.S.C. § 112, first paragraph

11. Previous rejection of Claims 37-38 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that "these claims have been amended such that they no longer recite the term portion but instead are directed to the specific trimeric complex" containing "HIV-1 gp120, D1D2 CD4 and Fab 17b", and argue that this "is adequately described in the subject specification" (see argument page 23, lines 7-11). However, as it is written, Claims 37-38 are not directed to the specific trimeric complex which satisfy the written description requirement. Amended Claims 37-38 are drawn to a genus of method using any polypeptide crystal comprising any variant of human HIV type I envelope glycoprotein gp120 as long as it contains amino acid residues 38-127, GAG, 195-302, GAG, 330-492, 1-182 from D1D2 domains of CD4, and Fab of 17b antibody. As disclosed in previous Office Action, "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (see page 10, middle of previous Non-Final Office Action). Thus, a genus of crystal encompassed by the Claims 37-38 do not satisfy the written description requirement as descirbed in the previous Office Action. For the reasons above, and as noted in the previous office action the instant rejection is maintained.

12. Previous rejection of Claims 37-38 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement is maintained, because the specification, while being

enabling for *in silico* screening of compounds using the full-set of atomic coordinates or a defined binding pocket within said full-set, as set forth in Figures 52-1 to 51-122, obtained from the X-ray diffraction data of a crystal consisting of the trimeric complex between fully deglycosylated HIV-1 gp120 construct Δ82ΔV1/2*ΔV3ΔC5, D1D2 sCD4 and Fab 17b (see Table 2, 4, 5 and 6 at pp.103-106), does not reasonably provide enablement to make and use a new polypeptide crystals comprising any variant of HIV Type I envelope glycoprotein gp120 as long as it contains amino acid residues 38-127, GAG, 195-302, GAG, 330-492, 1-182 from D1D2 domains of CD4, and Fab of 17b antibody.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that Claims are "directed to the specific trimeric complex between deglycosylated HIV-1 gp120, D1D2 CD4 and Fab 17b which the Examiner conceded is enabled by the subject specification" (see Remarks, page 25, lines 3-4). Although, it is true that the instant application has one specific polypeptide which is fully enabled. However, as it is written, the claims are drawn to method comprising use of a widely varying genus of polypeptide crystals as described above and in previous Non-Final Office Action. Thus, the one example disclosed in the specification does not satisfy factors that are considered in the previous office action, to practice a full scope of claimed genus in Claims 37-38. For the reasons above, the instant rejection is maintained.

New Rejections

Claim Rejections - 35 USC § 112

13. Claims 97-106 are rejected under 35 U.S.C. § 112, first paragraph, written description, for the same reasons noted in previous office action NO. 13 and herein for the same rejection of Claims 37-38.

14. Claims 97-106 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for the same reasons noted in previous office action NO. 14 and herein for the same rejection of Claims 37-38.

Maintained-Claim Rejections - 35 U.S.C. § 103

15. Previous rejection of Claims 37-38 under 35 U.S.C. § 103(a) as being unpatentable over Balaji *et al.* (US Patent 5,579,250, Balaji) in view *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that MPEP "§2116.01 applies to obviousness rejections under 35 USC §103(a), not MPEP §2106" as recited in the previous Office Action (see Remarks page 28, lines 3-5). However, the previous office action citing MPEP § 2106 was intended to provide additional information on patentable subject matters, which contains a computer-related nonstatutory subject matter in MPEP §2106.01, which is under §2106. Applicants argue "the Examiner has failed to establish a prima facie case of obviousness" (see Remarks page 27, bottom) and "All the limitations of claim must be

considered" and the prior art would have been obvious to one of ordinary skill in the art with a motivation. Applicant argue that Balaji et al. "does not teach the use of atomic coordinates of applicants' novel trimeric complex recited in amended claims 37 and 38" as recited in Remarks page 29, bottom. The instant Claims 37-38 are drawn to a method for identifying a compound capable of binding to the CD4 binding site of HIV Type I gp120 comprising steps of determining the CD4 binding site on gp120, comparing the structure of the CD4 binding site and determining whether the compound would fit into the binding site with non-functional descriptive material, i.e. three dimensional coordinate from the polypeptide crystal, which "does not distinguish the prior art in terms of patentability" as recited at the bottom of page 17 in the previous Office Action. Thus, "Nonfunctional descriptive material cannot render non-obvious an invention that would have otherwise been obvious" (see lines 11-12, page 18 in the previous Office Action). The method steps by the Balaji et al. disclosing a "rational drug design via computer modeling" as explained in previous Office Action (page 17, middle) disclose method steps describing all limitations encompassed by the instant claims method steps and the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art with a motivation "to develop drugs or compounds which interact" (see middle of page 17 in the previous office action) with a polypeptide or a protein. For the reasons above, the instant rejection is maintained.

New Rejections

Claim Rejections - 35 USC § 103

16. Claims 97-106 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Balaji *et al.* (US Patent 5,579,250, Balaji) in view *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) for the same reasons noted in previous office action NO. 15 and herein for the same rejection of Claims 37-38.

Summary of Pending Issues

17. The following is a summary of the issues pending in the instant application:

a. Claims 37-38 and 97-106 rejected under 35 U.S.C. § 112, second paragraph.
b. Claims 37-38, 97-98 and 101-104 rejected under of 35 U.S.C. 112, second paragraph.
c. Claims 37, 97, 99, 101, 103 and 105 rejected under of 35 U.S.C. 112, second paragraph.
d. Claims 37-38 stand rejected under 35 U.S.C. § 112, first paragraph, written description.
e. Claims 37-38 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.
f. Claims 97-106 are rejected under 35 U.S.C. § 112, first paragraph, written description.
g. Claims 97-106 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.
h. Claims 37-38 stand rejected under 35 U.S.C. § 103(a).
i. Claims 97-106 are rejected under 35 U.S.C. § 103(a).

Conclusion

18. Claims 37-38 and 37-106 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
January 4, 2007

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER